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FAMILY HISTORIES - HE'S OUR MIRACLE

Details

Written by Glenda Groff

Published: 17 July 2009

Quite a few parents were aware of Jordon Groff's illness this summer. His mother, Glenda , gives an account of this very trying time for the family and Jordon's progress since then.

Today is a damp, dreary day, and it is great to be here at home with our children. As I reflect on this past summer, it almost seems like a nightmare. Since the beginning of May, Jordan has been having a problem with constant vomiting. It would go in a cycle of about 3 to 4 days. He would vomit for several days, then be fine for a few days, then we would start all over again. During these times, he would have diarrhea and be very hyper. These were days of frustration for both doctor and mother.

I started keeping a chart of all the foods he ate and all the formula he drank. I also charted his activeness and any vomiting. Dr. Morton, being concerned that Jordan had Jardia, put him on Flagil. After the medication was discontinued, Jordan would seem fine for a week or two at the most. Then we would start the cycle all over again.

The beginning of August, after starting with a low grade fever and vomiting, Jordan was admitted to Lancaster General Hospital under the care of Dr. Morton. We felt we needed to get to the root of his problem, so tests were scheduled. On Aug. 8th he had an endoscopy, to examine his throat, stomach, and small bowel. Samples of tissue were also removed for testing. That day he was started on the TPN. Little did we know what the next few weeks would hold for our family.

Over the next days, tests began coming back. The good news was that they were negative, the bad news was that we were not getting any closer to the source of our problem. That following week, Jordan began running temperatures as high as 106E. More blood work revealed he had a

yeast infection in his blood stream, known as a Candida infection. At the time of the first blood culture, there were thousands of colonies in 1cc of blood. Our son was deathly ill.

He was put on a medicine know as Amphetarison, a very powerful one with some bad side effects. His kidney function and heart had to be closely watched. He was moved into a room close to the nurse's station and put on one-to-one nursing. That room became my home for the remainder of his stay. I began to feel like a dispatcher trying to get babysitters for our daughter and seeing that things were done at home.

After a few days, it was discovered that muscle pain went along with this illness. That explained why we could no longer hold him without his crying. He was the most comfortable lying on his back with his legs propped on a pillow. This was not the little boy we were used to-no smiles, no words, no more mischief dancing out of his eyes. Tests were run to find the source of the infection, but none was found. New problems cropped up. IV sites blew and become abscessed. A central line was inserted, solving that problem. Dr. Morton was able to concentrate the TPN, lessening the fluid overload that was starting to occur-another problem solved. Jordan's liver was enlarged, his pancreas inflamed, and blood had to be given.

On September 1st, Jordan was transferred to the Children's Hospital in Philadelphia. Dr. Morton wanted a second opinion on his illness. Jordan's amino acid levels had been pretty well under control until then, when it rose to 15 mg/dl. Tests were run and came back negative. We began to see a slight improvement.

Jordan's amylase was elevated, but they did not think it was high enough to have pancreatitis. They began to feed him, which made him worse again. Since they were not doing any more than Dr. Morton was doing, he was transferred back to Lancaster General Hospital. We were very grateful to have our son back under Dr. Morton's care.

Jordan definitely had pancreatitis, as he began vomiting more and more bile. His leucine level had dropped below 5 mg/dl. Dr. Morton began an IV. He needed to be on the TPN, but this was like feeding him, not allowing his pancreas to rest. He was put on a medication which aggravated his MSUD somewhat. After consulting other doctors, glutamine, alanine and aspartic acids were added to his TPN.

We began to see an improvement. Jordan began begging for a drink, but could not have any due to his constant vomiting. Finally, the day came when we were allowed to give 1/2 ounce. Once you gave him the cup there was no way you could get it back until it was empty. We gradually increased the amount to an ounce an hour.

Jordan's blood cultures were still coming back positive some of the time. He needed a stronger dose of medication. But when it was given at 1.5 mg/kg, his kidney function began to rise. He was lowered to 1 mg/kg.

By September 25th, Jordan had been weaned off the TPN, and was drinking formula. He still had an IV. Returning to the hospital the next morning, I remarked to my husband, "Maybe we can bring him home soon." Little did I know what we would find. As we walked into the room, the

nurses were trying to wake him up without success. I picked him up and his eyes would not open; he held himself stiff and cried. It reminded me of when he was a week old and sick from high levels.

Dr. Morton was called from surgery. Jordan had brain edema from which so many of these children die. He was immediately taken into the treatment room and given Phenobarbital and Manatol. Glutamine, which had not been added for 2 days, was added to the formula and given by Ng tube. Another IV was started and our little boy was put back on constant care nursing. They did an MRI the following day and it revealed an abnormal patterning of the Myelin. By the end of the week, he was back to what he had been before the brain edema. Through all this his highest leucine level was 11 mg/dl.

I had begun feeding him food, and what a mess! It was like trying to feed a baby, because he had a hyper gag reflex. We started with banana baby food and gradually added other foods.

We still had the problem of positive blood cultures. Out of 28 blood cultures, 18 were positive. Dr. Morton began working on getting an experimental drug, know as ABLC. One hundred and thirty-two people in the United States had used the drug with good results. On October 11th, the new medicine was given through an IV. It seemed to be just what Jordan needed. On October 14th he was sent home, ending a 65 day hospital stay. How wonderful home and the bed looked compared to the hospital room and cot.

We returned daily to the hospital for Jordan's medication through his central line. I had to feed him every 3 hours around the clock and flush his central line. As soon as I would pull syringes out of the kitchen cupboard, Jordan would come running saying, "My flushes." On November 4th, his medication was stopped and the central line pulled. That evening, he came to me and wanted me to flush his lines. It seemed he had forgotten that it was no longer there. He now had 32 days of negative cultures.

We never really discovered where the blood infection came from. Dr. Morton thought it was the result of a nutritional problem. Jordan became malnourished, weakening the lining of his mouth and throat, causing him to be vulnerable to the Candida infection. Dr. Morton thinks there are some amino acids that, to us, are non-essential, but to these children may be essential. We are hoping that Jordan's illness will bring new light to the problems that are faced by these children.

We are returning to the clinic weekly for checkups. On November 17th, Jordan returned to Lancaster General for an MRI to compare with the previous one. Dr. Morton and the radiologist were amazed at the difference. Where previously the patterning of the myelin was abnormal, this one looked normal. There definitely had been a fluid build-up. There were a few spots on the brain stem, ones that Dr. Morton feel will clear up with time. We know God is still in the business of doing miracles.

There are times when we look back wondering how we made it through, but we know that God promises that, "They that wait on the Lord shall renew their strength, they shall mount up with wings as eagles, they shall run and not be weary, they shall walk and not faint." We are very grateful to Dr. Morton and to God for the wisdom he has given Dr. Morton.

It is hard to believe all that Jordan has gone through when we see him running around and busy playing. He had to relearn nearly everything. The only difference we see is a small limp in his left leg, which Dr. Morton feels will clear up.

We apologize to the ones who felt neglected by all the time Dr. Morton spent on Jordan. We would never wish this on anyone. I feel inadequate in writing this, so maybe Dr. Morton will at some time write a more detailed article on his discoveries. The DNPH proved again it can be depended on as a very reliable test.

Jordan is doing great in his eating, his appetite has really increased. His favorite foods are French fries and spaghetti. I do not use any low protein foods at this time. He is now on glutamine and thiamine since coming home. Some days are still frustrating, but we are grateful to still have our son with us. May God be with you all.

FAMILY HISTORIES - NICK'S STORY

Details

Written by Karen Lovrin

Published: 17 July 2009

Diagnosed at the age of 10 2 months, doctors discovered Nick to be a medical mystery. His skin and blood tests indicated that Nick is a classic case of MSUD but should not have survived that long without severe disabilities or death. However, clinically Nick responds as a variant form of MSUD, a type all his own.

He is doing very well. Physically he has some tightness in the tendons of his legs, otherwise he is like the rest of the kids. He goes to physical therapy twice a week. After this month it will change to monthly visits since he's doing so well. He is 14 years old, slender and 5' 3". I have Nick in a private Christian school, mainly because he's not very motivated. He is a very social child and loves people. His school work ranges in the low to average scale. He loves sports, especially basketball.

Nick is seen every year or so by the University of California Medical Center (UCSF) in San Francisco. They try to follow him closely. Since he is a medical mystery, his tests are done for research and costs have been covered by the hospital. On these visits complete testing is done: blood work, X-rays, MRI and neurological tests, dietary and orthopedic check-ups, and psychological tests. It has been very encouraging, although we have had a few scares. Two years ago osteopenia (thinning of the bones) showed in the hand X-rays. Luckily this year there was no sign of it. The MRI does show some strange things, but it has not changed since the first one over 6 years ago.

I used to weigh and measure all Nick's foods, but now I just try to use good judgement. Nick is very good about his diet. Not that he's always happy he is on a restricted diet, but he knows the consequences all too well.

The first five years of his life were full of hospitalizations, only two extremely serious ones. He was flown down to UCSF by helicopter once and by airplane once. He is an excellent patient and has only whacked a doctor once. We still laugh about it.

When he was five years old, he spent a day with relatives and ate much more than he was allowed. After several hours in the hospital with an IV, we went home.

In the last five years Nick had two hospitalizations-once for the flu-once with fever. It seems the older he gets the less hospitalizations he needs. We handle most illnesses at home. Apple juice is a "lifesaver." Before the apple juice we used Pediatlyte. I just added Kool-Aid to it. I still get very worried and scared. We can't do much but work together and pray.

He has taken the MSUD Diet Powder since diagnosis. He does not like to drink it and mixes it as a thick milk shake. He uses it on his cereals and likes to dip and crunch up his potato chips in it. Without it, I notice quite a drop in his energy level. Nick eats a lot of potatoes (fixed every which way), vegetables, fruits and cereals.

Nick has some limitations. He tires easily. I have worked very hard at keeping communications open so that he lets me know at all times when he's not feeling right. I try to have consistent bed times and luckily Nick is a good eater.

It has been a learning experience raising a child with MSUD. It is only recently that I allow myself the luxury of thinking of a future for Nick. What profession will he be able to enter? Will he be able to marry and raise a family? So many questions. UCSF has just begun giving Nick genetic counseling. They will help teach him how to handle situations on his own and help him to better understand MSUD.

Nick's dream for the future is to be a basketball star. Isn't this the same dream as thousands of other little boys? I let Nick dream and one day we'll get down to reality. We have a computer in the bedroom and a hoop outside. He loves them both.

DR. MORTON RECOGNIZED WITH THE ALBERT SCHWEITZER AWARD

Details

Written by Cindy Stauffer

Published: 17 July 2009

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Dr. Holmes Morton, a county pediatrician and friend to "God's Special Children", received a national humanitarian prize in Baltimore Wednesday.

Morton, the founder and director of the Clinic for Special Children near Strasburg, received the Albert Schweitzer Prize for Humanitarianism in ceremony at the John Hopkins Medical Institutions.

Morton was awarded the $10,000 prize for his work among the Amish and Mennonite communities, treating children with genetic disorders. He was cited for practicing medicine in a compassionate way that respects the culture and lifestyle of his patients.

"Your presence as a tireless physician in a rural area, making house calls, has been received by these stricken families as a sign of providence," read the citation for the award. The Schweitzer Prize was created in 1986 by the Alexander von Humboldt Foundation of New York. Past recipients include President Jimmy Carter, author and editor Norman Cousins and Marian Wright Edelman, president of the Children's Defense Fund.

Morton, 43, is a graduate of Harvard Medical School. He has done extensive research in metabolic and neurological diseases, identifying about 40 different genetic disorders, including some that have never been described in medical journals.

"I am happy to have the work of the clinic recognized by the Schweitzer Prize," Morton said. "We try to provide medical care that is accessible and respects cultural beliefs. I hope the prize will make others more aware of the need elsewhere for the kind of care we provide here."

Morton, who was joined by his family at the award ceremonies, said he plans to use the monetary award to set up a special fund that will go on to support humanitarian work at the clinic.

THE CLINIC FOR SPECIAL CHILDREN

Details

Written by Joyce Brubacher

Published: 17 July 2009

Dr. Holmes Morton is the director and physician at a unique, nonprofit Clinic in Pennsylvania. The Clinic for Special Children now cares for more than 30 children with classic MSUD. Although the Clinic was founded as a local medical service to the children in Lancaster County, it is increasingly involved in the care of children in other states. Dr. Morton has consented to be a professional contact person for our

organization. I am confident he will be an asset to us.

The families who know Dr. Morton personally, are very pleased to see him honored with the Albert Schweitzer award (see following article, "Dr. Morton Recognized With the Albert Schweitzer Award"). He is a very caring doctor, totally dedicated to his patients and their families, giving of himself far above the call of duty. The families in turn have supported his work by donating land and their building skills to construct the Clinic. (See related articles in the April 1991 issue of the MSUD Newsletter.)

Upon receiving the award, Dr. Morton typically shares the recognition with others. In one newspaper article he was quoted as saying, "In a way, it's not so much a recognition of my individual work but the collective work of the people at the Clinic, and that includes the parents of the children I work with. It's a recognition of them, too."

The following accounts describe the benefit Auction and the Clinic for which it was held. The account of the Clinic is taken from an note of thanks written by the Clinic staff to a Mennonite church in PA.

Attending the Auction

On Sept. 18th Wayne and I attended the 3rd annual benefit Auction held in Leola, PA to support the Clinic For Special Children. The Clinic does not receive any money from the state or federal government, so this event is an important fund raiser.

We thoroughly enjoyed meeting the many PA families of children with MSUD and sharing the excitement of the huge crowd (over 5,000), 4 to 5 auction rings going all day, and the short speeches by Dr. Morton and Frank Allen, the former Wall Street Journal writer. (Frank Allen's articles on glutaric aciduria helped raise money to get the Clinic started.)

It was impressive to see the huge amount of donated craft items, 82 quilts and bakery carts stacked full of hundreds of tempting home-baked goodies. Smells from the concession stands and the barbecue pit outside stimulated our appetites. We could choose from a large variety of home style Pennsylvania Dutch cooking such as soft pretzels, chicken corn soup, shoofly pie and meadow tea.

Many items sold at very reasonable prices, except the item you had your heart set on, of course. "Excavator Wayne" decided he needed the special handmade wooden dump truck! The highest priced item this year was a dog kennel for $1 000, selling for a little less than last year's dog kennel. Last year a bedroom suite sold for $1100. The highest price paid for a quilt this year was $700 compared with last year's $800. Other higher priced items included a whirlpool tub, roll-top desk, utility shed and swing set. This is the third year for the Auction. The first year the event raised $78,000, the second year $95,000, and this year $105,000.

If you have the opportunity to be in PA next year (about the 3rd week in August), don't miss this very interesting and worthwhile Auction. Contact Enos Hoover for information on next year's Auction. Enos Hoover, 371 Grist Mll Rd., New Holland, PA 17557, phone: 717-354-

5415

- Joyce Brubacher

The Unique Clinic

The 1993 Benefit Auction for the Clinic For Special Children raised over $105,000 to help fund the Clinic's medical services and research on genetic disorders frequent to children of Amish or Mennonite heritage in Lancaster County. The funds from the Auction are essential to the Clinic's operation, but the moral support and encouragement expressed by so many in the conununity are also deeply appreciated by Dr. and Mrs. Morton and the Clinic staff. There are often long, difficult days for everyone involved in caring for children with unusual complex medical problems, but there is also a caring community. Thank you to all who participated to make the work of the Clinic possible.

The nonprofit Clinic depends on contributions to supplement its income from patient fees. This support helps cover the cost of maintaining its unusual laboratory equipment and diagnostic services, and provides support for Clinical research to improve the care and prognosis for children born with disorders such as maple syrup urine disease and glutaric aciduria, both potentially lethal disorders of protein metabolism.

With its unusual setting in the middle of an Amish farm, the Clinic has become one of the primary centers in the U.S. for diagnosis, clinical research and care of children with these metabolic disorders. It is the only facility of its type that combines pediatric primary care with highly specialized laboratory services to provide a coordinated approach in caring for children with metabolic disorders.

Contributions from the Auction every year help keep fees at reasonable levels so that all families who need them, including the testing for all Amish infants, can easily afford the Clinic's services. The Clinic is also involved in efforts to better understand and treat disease such as Amish nemaline myopathy, known to many as chicken breast disease. Funds from this year's Auction will also help the Clinic hire a needed, second, full time physician as soon as the right person for the job can be found.

MSUD AND OUR FRIENDS

Details

Written by Joyce Brubacher

Published: 17 July 2009

Another conversation at the picnic revealed an issue that I don't remember seeing addressed before. After her child with MSUD was born, a mother found a problem

developing with her best friend. When this mother spent time sharing with other parents of children with MSUD, her friend felt neglected. Others in our relationships also have to make adjustments and learn how to cope with this new development in our lives.

Since the picnic, I read a related article in the Vol.4, No.2 issue of the RTMDC News, a newsletter from England. I have briefly summarized the article, "Breaking the news to family and friends: Some ideas to help patients," by Helen McConachie a lecturer in Psychology at the Institute of Child Health, Meckleenburgh Square, London.

There is information available on how to break the news of a child's disease and/or disability to parents, but little is written on how to break the news to family and friends. Helen McConachie has drawn from various sources to offer suggestions and observations about breaking the news of a disability. These aptly apply to chronic diseases as well as disabilities. Following is a summary of the article.

Many elements can make sharing the diagnosis difficult. Parents own feelings will be very complex, and it is difficult to talk when you do not know clearly what you feel. Rejection may well be a part of their mixture of feelings. Parents may have been given, or may have taken in, very incomplete information about what is actually wrong with the child and what the future is likely to hold. In one instance, parents were not able to contact a related association until they had help explaining the baby's diagnosis to an older sibling.

Perhaps the hardest element of all for parents is knowing that their family and friends will experience feelings similar to their own; and since they can only just deal with their own feelings, they have no resources left to help others. Relatives and friends are frequently totally at a loss as to what to say, and their remarks can often seem awkward or unsympathetic.

Strategies to use:

- Be clear. If parents have communicated clearly and concisely with the professionals involved, and have written information to refer to, the task is made easier.
- Take a positive approach. Professionals should break the news in a way that allows for hope. Parents can then project a more positive approach to others.
- Discuss what to say. Professionals can help parents plan what to say and the appropriate level of discussion.
- Involve other parents. Other parents, especially with a similar child a little older, can help find the best words to explain the disability or disease. They can give emotional support when the family feels pressured by others to put on a "coping" face in public, or when close family members are so preoccupied with their own feelings they are less able to listen."
- Offer support. Professionals should be ready to offer a listening ear and help close family members keep from retreating into loneliness. Since parents cannot be expected, at an early stage, to provide much support for others in their families, setting up groups to meet others in similar situations can be of great help.

Conclusions:

When parents are told of a child's disability (or disease), they will need a network of supports. The success of the network depends somewhat on how parents break the news to their family and friends and how they cope with the consequent reactions. Grandparents, in particular, can be a source of strength or anxiety. Professional help should extend to enabling the whole family to function effectively and build up a solid network of social support in the community.

THE BIG PICNIC

Details

Written by Joyce Brubacher

Published: 17 July 2009

MSUD Reunion

We want to thank all who took time out of your busy schedules to come to the 1993 MSUD Reunion at the Grand Canyon of Pennsylvania. We were anticipating and working toward the picnic for so long. Now suddenly, it is history.

We really enjoyed the day. We found it impossible to do all the visiting we wanted to do.

We give special credit to our own families for taking a big part of the workload. We were eager to introduce them to our "MSUD family," and they were glad for the opportunity to be included.

The Lord blessed us with a beautiful day. The morning coolness in the shade soon turned to a comfortable temperature. It was interesting to see the group of people increasing. It wasn't long till you saw clusters here and there busily visiting. The group totaled approximately 200 people, twenty-two MSUD families with twenty-six MSUD children.

There were three out-of-state families, the Brubachers from Indiana, Walter Newswangers from New York, and the Silvas, who came the farthest, from Toronto, Canada. We thought it was a good turn-out, but we would have been happy to see more of those that couldn't come.

The biggest hurdle for the meal was the discovery that the electricity supply was not adequate for the demand. A few roasters needed to be taken back to a near-by home. A special thanks for all the food that was brought along. A woman's common worry about enough food was groundless.

The children spent a lot of time on the playground. After dinner, they tackled the challenge of

"fishing" for a surprise package.

The majority of the group hiked the one mile trail to the bottom of the canyon. After resting beside Pine Creek (some weren't satisfied till they fell in), we were ready for the climb to the top again.

We attempted to take a picture with all the MSUD children. It was quite a challenge. A few were sleeping and a few weren't there at the time. A morning picture might have been more successful.

Most everyone stayed for an early supper before heading home. A few families were camping.

We were sorry Dr. Morton and his family couldn't come. But we're grateful for his dedication to his patients. That was the reason for his absence.

We had the added bonus of doing some visiting the evening before the picnic. Wayne and Joyce Brubacher spent the night at our house. This was our first meeting in person. Also, Saul and Lucy Silva with their son Mark, came from their motel to enjoy Friday supper with us. Rebecca Huyard (Dr. Morton's office manager) spent from Saturday evening until Sunday afternoon with us. We enjoyed her stay and appreciated her helping hands.

Thanks for the contribution of everyone. Our efforts were rewarded.

- *John & Verna Mae Martin*

An Enriching Day-A Time of Sharing

Wayne and I attended the PA picnic in June. We thoroughly enjoyed ourselves at the lovely park with a wonderful day of visiting with the MSUD families. John & Verna Mae did an excellent job of organizing and providing the picnic.

The huge, delicious lunch included a large selection of low protein foods. (One 15 yr. old filled his pockets with low protein bars to be sure he would have some for his trip home.) In the afternoon we mothers kept "sampling" the low protein pretzels made by one of the Mennonite girls. A daughter of Ivan and Katie Fox worked in a pretzel factory and wanted to make a similar pretzel for her sister, Ruth. These are the hard, Pennsylvania Dutch type pretzels. (Recipe in Recipe section.) The adults probably ate most of them. They were as good as any pretzel I've ever eaten. Unfortunately, some children with MSUD are so very choosy, they wouldn't try them!

I took a few pretzels home for Shayla and she loved them. (Shayla could not go with us as it was the same day as the wedding of her good friend Rachel, and she had part in the wedding. (Rachel helped Shayla with the bread demonstration at the last Symposium.)

A highlight for me was a conversation after lunch with several mothers of teenagers and adults with MSUD. Various degrees of learning problems and the accompanying social challenges are

common in many older children with MSUD. We found a sympathetic audience as we voiced our experiences and frustrations.

I certainly don't want to be discouraging to any families. Not all persons with MSUD have these problems and the younger ones have the advantage of early diagnosis, new formulas and improved treatments. However, for us facing these challenges, sharing is informative and consoling.

We discussed issues such as how does one handle inappropriate behavior when reasoning and explaining seem to fall on deaf ears, or should I say, uncomprehending minds. For instance, how do you explain to adolescents why they are avoided at times by their peers, and being bold and demanding is not the solution?

It is hard for these children and young adults to develop close friendships, because they are very manipulative and possessive of persons showing them much attention. So parents are caught between a rock and a hard place, trying to protect children from the realities and cruelties of the world outside the family circle (and sometimes within families). Yet we also feel the need to protect others from our own manipulative, overbearing child. We find ourselves working two sides, thus feeling we are either doing an injustice to others or to our child. Each child is different and there are no easy solutions.

The fight for independence can be a real battle for any adolescent. For the youth with MSUD, the diet is one potential battleground. That can be very scary. The mother, especially, has a great deal of control over the child from infancy on. She is responsible for strictly controlling the diet and carefully monitoring the child for signs of illness and elevated levels. As one mother told me, the closer we are in our relationship with our child the more forceful may be the separation when the child seeks independence.

At our lively sharing session, some mothers frequently responded, "I know just what you are talking about." This sharing in groups and on a one-to-one basis is what these picnics and various gatherings are all about. We encourage parents in other areas to organize informal gatherings. Friendships take time to develop. Call or write letters to other families in our organization when it is not possible to meet personally.

Wayne and I have a concern for parents who feel they are alone in their trials. Each stage of child development has its challenges. We are especially concerned about those who suddenly withdraw from contacting other families in the organization during their child's adolescent years. You do not need to be alone during trying times.

Parents, we encourage you to share your experiences in the Newsletter. Just inform me if you do not want your name printed. We do not want to embarrass our children.

To the adolescents struggling with "growing pains," we welcome your stories. Maybe you find your family very helpful and would like to express your appreciation for their love, support and help. Share your feelings about having this rare disease. Is it just a natural, accepted part of your life or do you at times resent having to drink a special formula and restrict the foods you eat?

How do you cope with peer pressure? What advice do you have for others? How can others best help you?

Don't be concerned about how properly your letter is written. Please take time to write, or record what you have to say on a tape. Send it to me, the editor. I will type it for you.

- *Joyce Brubacher*

Comments About the Picnic

It was good for me to be with other moms to discuss our children's social behaviors. I don't feel so alone. - *A Mother*

I got to sit at the right table and I ate 5 whoopie pies!! - *Marlene Zimmerman (MSUD)*

The highlight for me was the hike to the bottom of the canyon with other parents, discussing our children's problems and progress. Sharing with other parents is always special. A big thanks to John, Verna and the other families for a great job! - *A Parent*

We really enjoyed the picnic, especially being with the other MSUD parents. Also enjoyed the hike to the canyon. - *Annie Hoover*

I liked fishing for candy and playing in the tire swing. I liked the rice and whoopie pies. - *Amy Zimmerman (MSUD)*

We really enjoyed it; was a nice place to have the picnic. The food selection was good. Good turnout! John and Verna and their families did a wonderful job! - Brenda Wenger

I had a lot of fun at the picnic. We should do it again soon. - *Idann Hoover (MSUD)*

I enjoyed the hike down to the canyon but not up! - *A Sibling*

We didn't know a lot of people, but we sure look forward to getting to know you better. We enjoyed the picnic and so did the children. We liked hearing the experiences of others; each one is different. - *Kevin & Dawn Hahn*

A BRIEF HISTORY OF MAPLE SYRUP URINE DISEASE (MSUD)

Details

Written by Richard J. Allen, M.D.

Published: 17 July 2009

Author's note: The 1990s were proclaimed by the President as the Decade of the Brain. The names of some, certainly not all, of the scientists who made significant contributions to the understanding of this unique metabolic disorder, I have indicated with parentheses. I believe this special decade is a symbol of the enormous benefit of Newborn Screening in recognizing rare metabolic disorders in children before clinical illnesses occurred that often brought them to medical attention. Unfortunately, prevention of brain damage (the cause of mental retardation, cerebral palsy, and epilepsy) has not achieved the recognition it deserves even in this very special decade. My award for this decade acknowledges all these little boys and girls, and their families, who permitted physicians to try to save their lives and "brains" with the limited scientific knowledge we had available.

In 1966, nearly 30 years ago, a two week old infant was transferred to the University of Michigan Hospital with suspected "meningitis." Bacterial meningitis, a central nervous system (CNS) infection, was always the first consideration in a suddenly sick infant. The little baby boy was very sick and in early stages of coma. At the time, no significance was given to a family history of a prior sibling who died in 1958 of an unknown cause. Infection was quickly eliminated in this child. There was not a peculiar "sweet" odor like maple syrup! However, the addition of 2,4-DNPH to the urine gave a strongly positive reaction. The urine also tested positive to Ferric Chloride (FeCl). Both tests were routine in my laboratory as a screen for possible metabolic disorders.

My research was focused on metabolic disorders, especially PKU. Both tests were positive, but FeCl gave a black-brown color rather than the expected "green" observed in PKU. The positive DNPH was also a "strong positive," giving an opaque yellow reaction.Another special test was then done on blood and urine specimens. My NIH grant provided a remarkable new instrument known as an amino acid analyzer. In 1954, the research of Moore, Spackman and Stein first reported the usefulness of this new method, column chromatography. This method permitted the precise quantitative determination of amino acids in small biologic specimens.

We pursued a thorough search of scientific literature. A paper, published in 1954 in a pediatric journal (Dr. J. Menkes) describing a progressive neurological disorder in a family affecting several children with an unusual substance in the urine, proved to be especially interesting. This disorder was one to be identified as maple syrup urine disease (MSUD). I later learned the author of the report, Doctor John Menkes, joined the training program at the Neurological Institute of Columbia University in New York a short time after I completed my training before returning to Ann Arbor.

In the early 1960s other investigators (Dr. J. Dancis) soon identified MSUD as a specific metabolic disorder due to an enzyme deficiency in the metabolism of a specific group of branched chain amino acids (BCAA) that accumulate in body tissues due to a presumed genetic deficiency of a specific enzyme. There had been some confusion about an unexplained increase in an unrelated amino acid, methionine. By refined chemical analysis

of specimens from affected patients, this proved to be another amino acid, alloisoleucine, that is unique to MSUD. (Drs. Norton and S. Snyderman)

Initial attempts to treat MSUD took place in London by Drs. Charles Dent and R. Westall in the early 60s. I had the great pleasure of a sabbatical research study in 1969 with Dr. Dent and colleagues (Dr. D.P. Brenton). Previous "visitors" from around the world in "Charlie's" lab included Drs. C. Scriver and M. Efron. His treatment plan with further refinements of the special formula (Drs. S. Snyderman, D. Lonsdale) was accepted. Removal of the BCAA from milk and foods was impossible, but mixtures of amino acids without the BCAA was successful.

Coincidentally, about the same time, another little baby boy was born at the other end of the country in Oregon in March of 1965 who also became sick in early infancy. When the family moved to Indiana, he came to Ann Arbor in 1967 to continue treatment begun in Oregon. Fortunately, he had been tested for MSUD by a new Guthrie test invented by Robert Guthrie, another science superstar in those early years of interest in metabolic diseases. He proposed Newborn Screening (NBS) for all babies, originally PKU and then MSUD. This began the era of NBS that has now been extended to all the United States and many countries around the world, especially for PKU, MSUD, Congenital Hypothyroidism (CH), and several other rare disorders. Yet in 1993, only 24 states have added MSUD to routine newborn screening panels.

These two babies were my first patients with MSUD. There were curious similarities in their lives and in the lives of the families. Both mothers subsequently had other pregnancies resulting in the birth of girls with MSUD. The mother of one had an amniocentesis in 1969 with cells sent to New York for special studies to determine whether the fetus was affected. Unfortunately the cells died during incubation, preventing the completion of tests to establish the diagnosis. That baby did have MSUD, which was established within hours of birth. Had the cells survived, this would probably have been the first inutero diagnosis of MSUD. Both were diagnosed by biochemical assay of newborn blood specimens in the first few hours of life in my laboratory. This allowed a special BCAA-free diet to be started extremely early in the life of these infant girls. They are now healthy, young adults who continue to use the special diet and monitor blood BCAA.

Back in 1966, the blood tests on this first MSUD baby indicated he had MSUD! We concocted a formula of amino acids, vitamins and minerals a little different from Dr. Selma Snyderman's. It was only several years later commercial producers of infant formulas began to provide such products for MSUD. The special formulas for infant PKU were still in trials at this time. Our clinic began to purchase large quantities of amino acids, formulated to our specifications, which we provided other clinics as well. This kept the costs down for families because this was not established treatment according to health providers. Many state public health departments should be acknowledged for stepping into the breech to assure formulas and services were available. This has been a struggle for all of us interested in treating infants affected with these rare disorders often discovered at birth by NBS. It is remarkable to me that while the cost of special formulas seemed quite great, health insurance providers have gradually acquiesced in the approval of other much more expensive child health costs (i.e., neonatal ICUs, organ transplant, etc.), but only to a limited degree for these remarkably beneficial treatment and cost-effective diets in MSUD and other similar disorders!

Nationally and internationally "science clubs" were formed, devoted to the biology of the new group of metabolic diseases designated Inborn Errors of Metabolism. The Society of Inherited Metabolic Diseases was organized in San Francisco in 1972. The first meeting of the Child Neurology Society was held in Ann Arbor in 1972. Parents of children with all types of neuro-metabolic disorders formed a "parent club" (Association of Neuro-metabolic Disorders) to advocate for their children. Contacts with other scientists around the world in the exchange of information about these then rare disorders helped us all to benefit the patients under our care. Babies and children were increasingly being recognized with MSUD. Parents also were advocates and organized families from around the world (Mr. & Mrs. Brubacher) to assure the provision of information and services for all known MSUD families. Physicians became aware that MSUD is among the many causes of neonatal coma. There are now several MSUD variants also. The knowledge of the enzyme defect, the genetics, and the neurology of this acute devastating disease has gradually been established (Drs. D. Danner, L. Elsas & C. Scriver). During acute bouts of metabolic decompensation with ataxia or coma, Total Parental Nutrition (TPN) is a great advance, avoiding the need for dialysis (Drs. G. Gaull & H. Berry).

In 1966 this first MSUD infant spent 8 months in the clinical research unit. Nutrition was a serious problem, with skin breakdown and failure to thrive apparently related to the malnutrition of a special formula lacking essential ingredients. The health of these first two boys was fragile and the intake of special formula a constant problem [for the one boy]. Intermittent bouts of acute illness intervened and occasionally required hospitalization [for the one boy, the other remained very healthy]. Fortunately, both these children had the devoted parents required for successful long term management. Frequent blood analyses required trips to the hospital for arm vein collections. Unfortunately, both boys died during metabolic crises near the end of the first decade of life.

Now newborn infants with MSUD are generally managed on an outpatient basis. Families simply send in a "Guthrie card" with a few drops of blood for the quantitative analyses of BCAA. Parents check the urine at home using DNPH. In clinical metabolic follow-up, Magnetic Resonance Imaging (MRI) is now available to better understand brain changes related to MSUD management. Recent MRI reports suggest these special dietary treatments do have an effect on brain development.

Dietary management still poses some problems; the composition of essential ingredients is not consistent in all formulas. Exact blood titration of individual amino acids during dietary modifications requires an efficient system of blood collection and analysis. Acute metabolic and neurologic episodes continue to be reported. Occasionally the sudden death of a seemingly healthy infant or child with MSUD occurs without explanation. The addition of thiamine has had variable success in clinical management. The neurological outcome appears to be very good, especially when the diagnosis is established early in life. However, there are still international reports regarding MSUD suggesting families and children have limited access to necessary medical care.

Those early days, even with the limited successes we were able to achieve, were very gratifying. I expect the outstanding, ongoing research in metabolism, neurology and genetics will change the care for these infants and children in the next few years. The prevention of mental retardation and brain damage from metabolic disorders is so much

more effective now as a result of many scientific contributors. The devotion and support of parents has been essential to the success achieved to date in caring for children with metabolic disorders. (Thanks, Moms and Dads.)

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